NOT FOR PUBLICATION

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

ACORDA THERAPEUTICS INC., Plaintiff, v. APOTEX INC. AND APOTEX CORP., Defendants.	)	Civil Action No. 07-4937 (GEB-MCA) **BENCH OPINION** **FILE UNDER TEMPORARY SEAL**

Table of Contents

BROWN, Chief Judge

This matter comes before the Court after a bench trial where Acorda asserted that Apotex infringes U.S. Patent No. 6,455,557 ("the '557 patent"). The patent is directed generally to using a tizanidine multiparticulate with food to reduce peak drug plasma concentration and severity of a side effect. Acorda markets tizanidine capsules under the trademark Zanaflex ®, which doctors use to practice the claimed invention. Apotex filed ANDA No. 78-868 with the Food and Drug Administration ("the FDA") seeking approval to market a generic version of the capsules.

This Court conducted a bench trial during seven days, between May 9 and May 24, 2011, with post-trial briefing completed on August 1, 2011. This opinion, including the legal discussion, constitutes the Findings of Fact and Conclusions of Law pursuant to Fed. R. Civ. P. 52(a).

The Findings of Fact contained in this opinion contain a number of factual findings which have been made upon completion of the bench trial. There was ample opportunity to examine the submissions of the parties and determine the credibility of the several witnesses after observing their demeanor and considering their relative interest, if any, in this matter.

Many of the Findings of Fact are substantiated with citations to testimony or documentary evidence or a combination thereof; such citations are not meant to be exhaustive authority for the finding. Some of the findings are based upon the record or inferences from the record which are not cited. All proposed findings of fact and conclusions of law inconsistent with those set forth herein are rejected.

I. FACTS

The Court's findings of fact are not limited to those in this section, but also include any credibility determinations or other determinations that appear below.

A. The Claims

This is a patent infringement case concerning the drug tizanidine, which is prescribed for a variety of purposes. Those purposes include the treatment of spasticity. When the drug is prescribed solely for spasticity, somnolence, essentially drowsiness, is an unwanted side-effect. The patent is directed to, among other things, using multiparticulate tizanidine with food to reduce somnolence. (U.S. Patent No. 6,455,557 ("the '557 patent") at 14:8-34). However, the drug is used for many other purposes, including to create drowsiness. (5/9/11 AM tr. at 108-109; 5/10/11 AM tr. at 69; 5/10/11 PM tr. at 5-7; 5/23/11 PM tr. at 75, 81-89, 95-96).

Acorda contends that Apotex infringes claims 1-21 of the '557 patent by inducement because it encourages doctors to practice the claims. A summary of the claims is not difficult. Claim 1 claims:

> A method of reducing somnolence in a patient receiving tizanidine therapy comprising[:]
>
> [1] administering to the patient a therapeutically effective amount of tizanidine in
>
> [2] an immediate release multiparticulate pharmaceutical composition with food,
>
> [3] wherein administration of the composition with food produces a peak plasma tizanidine concentration earlier than about 4 hours from administration.

Claims 2 and 3 depend directly on claim 1 and narrow this method to a specific dosage—between 0.5 mg and 12 mg, and between 2 mg and 8 mg respectively. Claims 4, 5, and 6 also depend on claim 1, and further limit claim1 based upon how close the dosage must be taken to the time of eating. Claim 4, requires the administration to occur between "30 minutes prior to 2 hours after consuming food"; claim 5 requires the administration to occur "substantially at the same time as the consumption of the food"; and claim 6 requires that the administration occur "immediately after the consumption of food up to 1 hour after said consumption." ('557 patent at 14:8-35).

Claims 7-9 are dependent claims claiming the preferred "tizanidine on beads" formulation. Claim 7 narrows the immediate release multiparticulate to be in the form of "tizanidine on beads." Claim 8 further narrows claim 7 by requiring the drug be administered using a "unit dosage form." Claim 9, further narrows claim 8, by requiring the unit dosage form to contain from "2 to 6 milligrams of tizanidine." (*Id.*).

Claim 10 is similar to claim 1, except that the object of its method is to reduce peak plasma concentration ("Cmax") from an oral dosage as opposed to reducing somnolence. It claims:

> A method of reducing the peak plasma concentration from an oral dosage form of tizanidine in a patient in need of a therapeutic effect thereof comprising:
>
> [1] administering to the patient a therapeutically effective amount of tizanidine
>
> [2] in an immediate release multiparticulate pharmaceutical composition with food,
>
> [3] wherein administration of the composition with food produces a peak plasma tizanidine concentration earlier than about 4 hours from administration.

Claims 11 and 12 narrow this method to using a specific dosage—0.5 mg to 12 mg and 2 mg to 8 mg respectively. Claims 13, 14, and 15 narrow claim 10 with the same language used in claims 4, 5, and 6—they narrow the timing of what it means to take the multiparticulate "with food" to certain time periods. ('557 patent at 14:35-63).

Claims 16-18 also claim the preferred "tizanidine on beads" embodiment. Claim 16 narrows claim 10 by requiring that the multiparticulate be "tizanidine on beads." Claim 17 narrows claim 16 in a similar way as described by requiring the method be practiced with a "unit dosage form." Claim 18 narrows claim 17 further by requiring the unit dosage to contain from 2 to 6 milligrams of tizanidine. (*Id.*)

Claim 19 is an independent claim to "a method of reducing the peak plasma concentration from an oral dosage form of tizanidine in a patient in need of a therapeutic effect thereof comprising":

> [1] administering to the patient a therapeutically effective amount of tizanidine
>
> [2] in an immediate release multiparticulate pharmaceutical composition
>
> [3] with food,
>
> [4] wherein the composition produces a peak plasma tizanidine concentration earlier than about 2 hours from administration when administered without food.

('557 patent at 14:63-15:2). In other words, it is similar to claim 10, except that it is "the composition" that produces peak plasma in "2 hours" when administered *without* food.

Claim 20 is also an independent claim directed to "a method of reducing the peak plasma concentration from an oral dosage form of tizanidine in a patient in need of a therapeutic effect thereof comprising":

> [1] administering to the patient a therapeutically effective amount of tizanidine

> [2] in an immediate release multiparticulate pharmaceutical composition
>
> [3] with food,
>
> [4] wherein the composition releases substantially all of its tizanidine contents within 60 minutes of administration.

('557 patent at 15:4-11). Claim 20 is similar to claim 19, except that its time limit is "60 minutes" and its final element focuses on the release of the tizanidine contents, not the peak plasma concentration.

Claim 21 is the last claim of the patent and is an independent claim directed to "a method of reducing the peak plasma concentration from an oral dosage form of tizanidine in a patient in need of a therapeutic effect thereof comprising":

> [1] administering to the patient a therapeutically effective amount of tizanidine
>
> [2] in an immediate release multiparticulate pharmaceutical composition
>
> [3] with food,
>
> [4] wherein the composition releases at least 75% of its tizanidine contents within 60 minutes of administration.

('557 patent at 16:1-9). This claim is similar to claim 20, the only difference being that it requires that "75%" of the tizanidine releases its contents in the 60 minute period.

In the claim construction proceeding, the Court found that each claim preamble was limiting and concluded that the following definitions applied to the terms:

> "reducing" means lessening, decreasing, or diminishing;
>
> "somnolence" means drowsiness or the inclination or propensity to fall asleep;
>
> "tizanidine therapy" means a course or regimen of, or need for, treatment involving an individual taking a pharmaceutical composition containing tizanidine for treatment of spasticity;

> "administering" means giving, prescribing, dispensing, dosing, self-dosing or taking and is separate and distinct from the term "administration";
>
> "immediate release" means a composition which allows all or substantially all of the tizanidine to be released from the dosage form in less than 60 minutes;
>
> "multiparticulate pharmaceutical composition" means a plurality of discrete particles, pellets, mini-tablets and mixtures or combinations thereof;
>
> "with food" means the consumption of solid food from 1 hour before administration to 2 hours after administration of the multiparticulate dosage form recited in claims 1, 10, and 19-21;
>
> "administration of the composition" means the giving, dosing, self-dosing or taking of the claimed composition and is separate and distinct from the broader claim term "administering";
>
> "produces a peak plasma tizanidine concentration earlier than about 4 hours from administration" means that the composition is designed to provide a Cmax (maximum concentration of a drug in the human blood plasma of an individual) of tizanidine in an individual in less than about 4 hours. The term does not refer to the average maximum plasma concentration of the drug for a group of individuals;
>
> "tizanidine on beads" means an immediate-release composition containing seeds and tizanidine,
>
> "releases substantially all of its tizanidine contents within 60 minutes of administration" means that the claimed composition releases greater than 75% of its tizanidine from the dosage form within 60 minutes after it is taken;

(*See* Doc. No. 85). Importantly, the Court construed "tizanidine therapy" and determined that it referred to the treatment of spasticity, not all possible conditions that use tizanidine therapy. Further, the Court rejected Apotex's construction of "reducing," which would have required a statistically significant reduction in a group of individuals and instead adopted Acorda's definition and allowed a reduction in a single individual to satisfy infringement.

B. The Specification

The patent's specification discloses a single study, which the parties refer to as the "101 study." The full study is not reported in the patent, but the patentee did include a more limited write-up of the study. (*Compare* '557 patent, *with* DTX25). That study was a 4-way cross-over study that used the same patients and compared the blood plasma concentrations of tizanidine capsules, as represented by 2x4 mg capsules manufactured by Elan Pharmaceutical Technologies, Lot No. PS1066P, in the fed (Treatment C) and fasted (Treatment D) state and also gave test subjects two 4mg tablets, as represented by Brecon Pharmaceutical Limited's Lot No. 197MFD1299, in both the fed and fasted state. ('557 patent at 6:43-61). However, as brought out at trial, Elan Lot No. PS1066P, was, like every example in the patent, a tizanidine-on-beads formulation, not any other kind of multiparticulate. (DTX129 at 24, 50; DTX 11 at 5-6; 5/10/11 PM tr. at 82-84).

The results reported are reproduced below:

TABLE I

Pharmacokinetic Data
Tizanidine Tablet/Capsule Study

PARAMETER	Treatment A	Treatment B	Treatment C	Treatment D
T_{max} (hr) Median value	1.41	1.00	3.00	1.01
C_{max} (ng/mL) Mean value	6.80 [0.25]	5.43 [0.25]	4.57 [0.25]	5.36 [0.25]
AUC_{last} (ng * hr/mL) Mean value	20.31 [0.99]	15.78 [0.99]	17.43 [0.99]	15.99 [0.99]
AUC_{inf} (ng * hr/mL) Mean value	22.08 [1.82]	19.54 [2.01]	20.83 [2.54]	18.01 [2.12]

Treatment:
A = 2 × 4 mg Tizanidine Tablets with food
B = 2 × 4 mg Tizanidine Tablets without food
C = 2 × 4 mg Tizanidine Capsules with food
D = 2 × 4 mg Tizanidine Capsules without food
Values in brackets are the standard error

('557 patent at 8:1-21). The mean Cmax was lower for treatment C than treatment D, and was lower than either tablet level. The specification makes only the following statement about the somnolence results: "There was no impairment at 0.75 hours following capsules taken under fed conditions while the impairment was significant with the other three dosing groups. At 1.5 hours and 2.5 hours post dose, performance was impaired under all four dosing groups to a lesser extent than at 0.75 hours and the effect resolved completely by 6 hours past dose. The secondary measures showed the same pattern of change as "Power of Attention." ('557 patent at 7:52-64).

The specification also contains a series of examples of the formulation. These examples varied in excipients and in preparation, but all were tizanidine on beads formulations.

C. Contentions Related to Direct Infringement

Apotex's (non-invalidity-related) case focuses on undermining Acorda's proof with respect to three limitations in the patent:

> (1) Apotex contends that its product is not a "multiparticulate pharmaceutical composition" and thus does not infringe any of the claims because all the claims contain that limitation.
>
> (2) Apotex contends that Acorda has not shown that administering Apotex's product with food reduces Cmax, which would prevent Apotex from infringing claims 10-21, which require reduction of peak plasma concentration;[1]
>
> (3) Apotex contends that Acorda has not shown that administering Apotex's product with food reduces somnolence, which would prevent Apotex from infringing claims 1-9, which require reduction of somnolence.

[1] The Court ruled at the *Markman* hearing that the preambles to the claims were limiting. (*See* Doc. No. 85).

The status of infringement is as follows for demonstrative claims 1 and 10, with a checkmark meaning that Apotex does not seriously dispute the presence of that element in its ANDA product for the purposes of infringement, and a question mark meaning that Apotex contests the presence of that element:

CLAIM 1 **Claim Element**	**Present in ANDA Product?**
A method of *reducing somnolence*	
in a patient receiving tizanidine therapy comprising[:]	
[1] administering to the patient a therapeutically effective amount of tizanidine in	
[2] an immediate release *multiparticulate pharmaceutical composition* with food,	
[3] wherein administration of the composition with food produces a peak plasma tizanidine concentration earlier than about 4 hours from administration	

CLAIM 10 **Claim Element**	**Present in ANDA Product?**
A method of *reducing the peak plasma concentration*	
from an oral dosage form of tizanidine in a patient in need of a therapeutic effect thereof comprising[:]	

[1] administering to the patient a therapeutically effective amount of tizanidine in	
[2] an immediate release *multiparticulate pharmaceutical composition* with food,	
[3] wherein administration of the composition with food produces a peak plasma tizanidine concentration earlier than about 4 hours from administration	

The Court will refer to claim 1 and the claims dependent thereon, claims 1-9, as the "somnolence claims" because each of them is directed to reducing somnolence in a patient receiving tizanidine therapy. The Court will refer to claims 10-21 as the "Cmax claims" because they are directed to reducing peak plasma concentration.

D. Person of Ordinary Skill in the Art

At trial, the parties agreed that the relevant art was that of pharmaceutical formulation in November of 2001 (the filing date of the '557 patent). The parties further agreed that the person of ordinary skill in the at art would have a Ph.D. in pharmaceutical sciences, or a related field, with three to five years of experience in the pharmaceutical industry, or an appropriate bachelor's or master's degree and about seven years of experience formulating drugs. (5/1/112 PM tr. at 51-52; 5/23/11 AM tr. at 23-24).

II. EVIDENTIARY ISSUES

There were two evidentiary issues that the parties briefed before the Court during the trial. The first is the admission of DTX129. The document was produced by Acorda's

predecessor in interest in the patent, Elan Pharmaceuticals. Acorda objects to its admission based upon its assertion that the document lacks authentication. The Court disagrees.

"[T]he burden of proof for authentication is slight." *United States v. Reilly*, 33 F.3d 1396, 1404 (3d Cir. 1994). All that is required is "a foundation from which the fact-finder could legitimately infer that the evidence is what the proponent claims it to be." *In re Japanese Electronics*, 723 F.2d 238, 285 (3d Cir. 1983). That evidence may come from the "appearance, contents, substance," of the document being authenticated, FED. R. EVID. 901(b)(4), or through circumstantial evidence. *McQueeney v. Wilmington Trust Co.*, 779 F.2d 916, 930 (3d Cir. 1985). The testimony of a witness is not necessary to authenticate a document. FED. R. EVID. 903.

The Court finds that Apotex has met its burden of proving authentication. Here, the document contains sufficient reliability to suggest that it is what the proponent claims it to be. For the following reasons, circumstantial evidence and comparison to documents that have been authenticated are sufficient for this document:

- DTX 129 describes tablets "manufactured by Brecon Pharmaceutical Limited, Lot No. 197MFD1299, expiration date, Dec. 31, 2004," information that is identical to that contained in the authenticated '557 patent. (DTX 129 at 16, '557 patent at 6:55-57).

- DTX 129 describes a 2 mg multiparticulate capsule containing tizanidine HCl (2.29 mg), hydroxypropyl methylcellulose 3 cps (3.16 mg), silicon dioxide (1.05 mg) and non pareil beads (68.7 mg), which are the identical excipients and amounts as those contained in Table 2 of the '557 patent. (DTX 129 at 25 and 50, '557 patent at table 2).

- There are numerous other duplications between the two documents.

- While Elan, a third party, produced this document in this case, Acorda produced very similar documents in this case. There are differences between the documents, but they are distinctly similar. (*Compare* PTX6 *with* DTX129).

Further, the producing party, Elan, was the predecessor to *Plaintiff* and acts as its manufacturer. It has utterly no incentive to forge this document. The Court thus admits the document in evidence.

The other evidentiary issue is that Apotex contests much of the testimony of Lauren Sabella as hearsay and double-hearsay that is not within a relevant exception.[2] There were two kinds of statements reported by Ms. Sabella: the first were statements from a single doctor about his thoughts on the perceived benefits of Zanaflex Capsules; the second were statements made by doctors about their perception of the advantages of Zanaflex capsules to sales representatives whose statements were then reported to the regional sales advisory team, and then to Ms. Sabella. (5/10/11 AM tr. at 17). The Court finds that the first set of statements are admissible, but the second set of statements are not.

Evidence of a declarant's then-existing mental, emotional, or physical condition is admissible over a hearsay objection. Federal Rule of Evidence 803(3) states that evidence is admissible over a hearsay objection if it is:

> A statement of the declarant's then-existing state of mind, emotion, sensation, or physical condition (such as intent, plan, motive, design mental feeling, pain, and bodily health), but not including a statement of memory or belief to prove the fact remembered or believed[.]

(Emphasis added). The Court agrees that the "intent" exception allows Sabella's testimony to pass through the first level of hearsay. The statement by the doctor on Sabella's ride-along was a statement of his intent to use the capsules in a certain way. Thus, that evidence is admissible.

However, there is another, and in many cases, two other levels of hearsay involved in other portions of Sabella's testimony. This next level of hearsay occurs when the sales

[2] Acorda's argument that Sabella's memories qualify as business records because they are communicated in the course of business by someone with knowledge is meritless. No corporation keeps *records* in the memories of their staff. Indeed, the need to keep records arises because human memory is flawed. As such, a person's recollection of statements made to them can hardly be a "memorandum, report, record, or data compilation." FED. R. EVID. 803(6). Indeed, Ms. Sabella stated in her testimony that the feedback is not generally recorded. (5/10/11 AM tr. at 16).

representative tells the regional sales advisory team that "Doctors understand from the label that they should use Zanaflex capsules to reduce Cmax and somnolence." Now, the statement must be taken for the truth of the matter asserted—otherwise it has no relevance because if the statement is false (i.e. Doctors do not so understand); it does not support Plaintiff's case. Nor is it the statement of the declarant's (here the sales representative's) state of mind. Further, there is another level of hearsay when the regional sales advisory team conveys the information to Sabella.

Acorda argues that Sabella could testify to her experience, simply saying that she has received numerous reports of doctors understanding the label in this manner. However, the Court does not see the relevance of this information unless the underlying statements communicated to her are true and is not persuaded by Acorda's arguments.

Even if these statements were not hearsay, the Court would afford this portion of Ms. Sabella's testimony little, if any, weight. The Court sees no reason to rely on third or fourth-hand verbal knowledge. This is particularly true when there were surveys conducted of physicians before the Court. (*See* PTX255 at ACO 35288-92). The Court will not put much reliance on statements made in situations where there is no record of the context in which these statements are made, and where the representatives could easily have given information that went beyond what was available in the label. Further, the marketing materials used in these visits, while they contained similar sentences to the label, did not in fact rely primarily on the label itself.

III. DISCUSSION

A. Infringement Standard

"A patentee claiming infringement must present proof that the accused product meets each and every claim limitation." *Forest Labs., Inc. v. Abbot Labs.*, 239 F.3d 1305, 1310 (Fed. Cir. 2001). If a limitation is missing in the accused product, literal infringement is not present. *See Kraft Foods, Inc. v. Int'l Trading Co.*, 203 F.3d 1362, 1370 (Fed. Cir. 2000).

However, "[e]ven if an accused product differs enough from an asserted claim to preclude literal infringement, that product may infringe under the doctrine of equivalents if there is equivalence between those elements of the accused product and the claimed limitations of the patented invention that are not literally infringed." *Zelinski v. Brunswick Corp.*, 185 F.3d 1311, 1316 (Fed. Cir. 1999) (citing *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 21 (1997)). There are two tests for the doctrine of equivalents. First, an element of an allegedly infringing instrumentality is equivalent to an element of the claims when there is "substantial identity of function, means, and result." *Id.* Second, a limitation may be equivalent if the differences between the claimed element and the purportedly corresponding infringing element are insubstantial. *Abraxis Bioscience, Inc. v. Mayne Pharma (USA) Inc.*, 467 F.3d 1370, 1382 (Fed. Cir. 2006); *Honeywell Intern. Inc. v. Hamilton Sundstrand Corp.*, 370 F.3d 131, 1139 (Fed. Cir. 2004).

The doctrine of equivalents "does not require complete identity for every purpose and in every respect[.]" *Lear Siegler, Inc. v. Sealy Mattress Co. of Mich., Inc.*, 873 F.2d 1422, 1425 (Fed. Cir. 1989). However, the doctrine of equivalents is a limited doctrine. It was "designed to protect inventors from unscrupulous copyists and unanticipated equivalents" and should not be applied so broadly that it becomes "the second prong of every infringement charge, regularly

available to extend protection beyond the scope of the claims[.]" *Kinzenbaw v. Deere & Co.*, 741 F.2d 383, 389 (Fed. Cir. 1984); *Charles Greiner & Co. v. Mari-Med Mfg.*, 962 F.2d 1031, 1036 (Fed. Cir. 1992). Further, the doctrine should never be used to vitiate a claim term because potential competitors should be able to rely upon the language of the patent claims. *Charles Greiner*, 962 F.2d at 1036; *Zodiac Pool Care, Inc. v. Hoffinger Indus., Inc.*, 206 F.3d 1408, 1416 (Fed. Cir. 2000).

B. Analysis

The Court will first address the infringement of claims 7-9 and 16-18, the claims that contain the limitations "tizanidine on beads" under the doctrine of equivalents. Then the Court will proceed to the common issues involved in the Cmax and somnolence claims that do not include this limitation.

1. Apotex's ANDA Product Does Not Infringe Claims 7-9 and 16-18 Under the Doctrine of Equivalents

The Court construed "tizanidine on beads" as "an immediate-release composition containing seeds and tizanidine." (Doc. No. 85). Acorda manifestly failed to carry its burden as to whether Apotex's formulation infringes these claims under the doctrine of equivalents. To read "tizanadine on beads" to include a granulation would vitiate a claim term and render claim 7 effectively equivalent to claim 1, from which it depends.

Both parties agree that Apotex's capsule product is not filled with beads, but with a granulation. Dr. Jarosz testified that Apotex will make its product using roller compaction, a dry granulation process that does not involve further processing. (5/1/11 PM tr. at 87; PTX10 at 000245-249, 253). As a result, the product results in a granulation with substantial powder, not

beads, which require a seed and a coating of drug product. Nonetheless, Acorda contends that Apotex's product infringes by the doctrine of equivalents.

Acorda's testimony on the matter does not follow the "function-way-result" test because its expert, Dr. Williams, testified that he did not know the "way" in which the tizanidine on beads accomplished their object. (5/9/11 PM tr. at 20-22). Nor did he know the way Apotex's powdered granulation functions. (*Id.* at 22). Instead, Dr. Williams testified that the two were "interchangeable" because Apotex's product was bioequivalent to Zanaflex Capsules. (5/9/11 AM tr. at 160-161).

However, this testimony is manifestly insufficient. Testimony as to the doctrine of equivalents must focus on an element by element basis and the "role played by each element in the context of the specific patent claim." *Warner-Jenkinson Co.*, 520 U.S. at 40. "[G]eneralized testimony as to the overall similarity between the claims and the infringer's product . . . does not suffice." *American Calcar, Inc.v. American Honda Motor Co., Inc.*, ____ F. 3d ___, at *14 (Fed. Cir. 2011). Dr. William's testimony violated both tenets; it focused on the effects of the formulation as a whole, not on the "tizanidine on beads" aspect. Thus, it did not address the particulars of the element and its role, as opposed to those of taking the formulation with food or its general "multiparticulate" nature. Further, the fact that Apotex's products are "bioequivalent" does not suggest that they are truly interchangeable within the meaning of the patent—indeed bioequivalence requires only that the pharmacokinetic data be within 80% to 125% of the Acorda formulation in both the fed and fasted state. (DTX150; 5/12/11 PM tr. at 77, 80-83). It thus addresses only the product as a whole and not the individual element, and Acorda manifestly failed to carry its burden.

Further, the Court finds Dr. Jarosz's unrebutted "function-way-result" testimony to be convincing. Jarosz demonstrated that the way that the two formulations function are substantially different. Jarosz testified that Apotex's product uses a pH-dependent polymer called PVAP to modify the release of tizanidine when the stomach is in the fed state. (5/12/11 AM tr. at 7, 13-16; DTX 97 at 8-10; Joshi Tr. at 49-53). By contrast, the tizanidine-on-beads limitation uses beads of uniform size, shape, and drug content that cause different pharmacokinetic profiles depending on whether the stomach is in the fed or fasted state. (5/12/11 AM tr. at 12-16). The Court finds that this difference is not "insubstantial" and prevents a finding of equivalence.

The Court acknowledges that every difference does not prevent doctrine of equivalents from operating and that the purpose and context of the claim term affect the scope of "substantial" similarity. An elephant and a mouse are substantially similar for the purposes of being mammals and of being important Disney characters, but not substantially similar for the purposes of transporting cargo or attacking ancient Rome.

In this case, the difference is substantial, particularly in light of the fact that "tizanidine on beads" is narrowed from the previous claim of "multiparticulate," suggesting that merely being a multiparticulate is not sufficient to be "tizanidine on beads." To apply the doctrine of equivalents to the conventional granulation would vitiate the claim term "tizanidine on beads" and make its claim scope the same as, or larger, than the claim from which it depends. *See Charles Greiner*, 962 F.2d at 1036.

2. Apotex's ANDA Product Is a Multiparticulate

Acorda contends that Apotex's granulation is a multiparticulate as that term is used in the patent. The Court construed the term "multiparticulate pharmaceutical composition" in the

Markman hearing to mean: "a plurality of discrete particles, pellets, mini-tablets and mixtures or combinations thereof." (Doc. No. 85).

Apotex's product is made from a granulation, (5/1/11 PM tr. at 87; PTX10 at 000245-249, 253), by a roller compaction process. Apotex's roller compaction is a dry granulation process, which runs the blended powder through two rollers to create a granulation and then through sieves to select the proper ratio of fines, and other sizes of granules. While Apotex's Dr. Jarosz agrees that some granulations can result in multiparticulate, he testified that Apotex's granulation does not undergo the additional processing required to be a multiparticulate. (5/10/11 PM tr. at 52-57, 60-64, 74-79; DTX10 at 6-7). Apotex's product, once removed from its capsule is depicted in the pictures below:


APD T2

(DTX 98). As can be observed easily from the pictures, the particles blend into one another and include a substantial amount of fine powder as well as larger conglomerate lumps of varying sizes. (5/10/11 PM tr. at 89-96). To the naked eye, the particles do not appear to be discrete—there is no clear separation between the particles and there is a substantial fine powder. Indeed, these capsules are made by dry granulation processes, (DTX97 at 00020; DTX 123), which allows for the capsule dosage form to contain up to 80% fine powders. (*See* 5/10/11 PM tr. at 89-96; DTX 97 at 27). Both parties' experts agreed that powdered formulations are not "multiparticulate pharmaceutical compositions." (5/12/11 AM tr. at 112; 5/23/11 AM tr. at 28).

However, the fact that these particles are not discrete to the naked eye does not mean that they are not discrete within the meaning of the art. Indeed, Dr. Jarosz himself described the particles as discrete:

> [A:] It has powder, there are powder components, there's granules, there's varying multitude of sizes, yes. It is a size range from, say this being the largest particle, I'm pointing out a particle specific on the panel.
> Q That's over on the left hand side and near the top of the powder?
> A Yes.
> Q Thank you.
> A And, then there are powder -- **discrete particles that are of varying sizes.** That would be exactly what I would expect being retained, either on the 40 or 60 mesh screen, the 80 mesh screen, the 100 mesh screen, the 200 screen.
> Q And, are there any fines shown in that picture?
> A Yes, of course. There's many fines. And probably, it's hard with this magnification to see the fines, but one can think of specks, dust specks, and these elements down in here, are the visual representation of those very, very fine particles.

(5/10/11 PM tr. at 95-96) (emphasis added). The Court credits this testimony because it was against the interests of Apotex for its witness, Dr. Jarosz, to so describe the dry granulation. Further, he was looking at these pictures when he made the statements. Thus, it appears that Dr. Jarosz believes that the picture contains discrete particles, but simply believes that they are not

multiparticulates because the discrete particles are not of consistent size. (5/10/11 PM tr. at 87-92, 94-96; 5/12/11 AM tr. at 16).

However, the Court finds that the testimony that multiparticulates must be of consistent size is not credible for three reasons: (1) it is inconsistent with the Court's construction and the patentee's express definition of the term in the patent; (2) Dr. Jarosz was unable to produce any scientific literature to support the fact that multiparticulates *must* be of a consistent size and literature supported some variation; (3) his comportment on the stand suggested that he was not being forthright with the fine distinctions facing the Court.

First, it is clear that Dr. Jarosz's opinion is based on his perspective as a person in the art. However, the *general* definition in the art is not at issue in this case. The patentee acted as his own lexicographer, and defined "multiparticulate pharmaceutical compositions" to mean "a plurality of discrete particles, pellets, mini-tablets and mixtures or combinations thereof." As shown above, it appears that Dr. Jarosz believed that Apotex's product contained discrete particles of varying sizes. (5/10/11 PM tr. at 95-96).

The argument that generally "multiparticulates" may not include particles of varying sizes is not convincing, because the definition in the patent does *not* include that limitation. As redefined, that term only requires "a plurality of discrete particles . . . or combinations thereof;" no reference is made to the size of those particles. ('557 patent at 4:21-27; Doc. No. 85). Thus, as defined by the patentee and the Court, no such limitation is required. Further, there is no doubt that "mixes" of particles and pellets as contemplated in the patentee's definition would have different sizes.

Second, it is clear from the literature that even for the general definition of "multiparticulate," that while there is a preference for consistent sizing, there is substantial

tolerance on the variance in the size of the particles. (*See, e.g.*, U.S. Patent No. 7,776, 314 ("The multiparticulate forms *preferably* have a *size in the range* from 0.1 to 3 mm, particularly preferably in the range from 0.5 to 2mm"); U.S. Patent No. 4,981,468 ("Drug particles prepared by wet or dry granulation techniques often possess an irregular surface and a relatively wide particle size distribution."); U.S. Patent No. 7,741,334 ("The melt-extruded multiparticulates can be about 0.1 to about 12 mm in length and have a diameter of about 0.1 to about 5 mm."). Dr. Jarosz presented no scientific articles that suggested that each type of multiparticulate must have a consistent size. Thus, the term "multiparticulate" in the Court's construction includes Apotex's granulation.

The Court also grants some limited weight to the testimony of Acorda's expert. Acorda's expert, Dr. Williams, never saw Apotex's product, despite several examples having been sent to Acorda. (5/9/11 PM tr. at 10). Nonetheless, Dr. Williams testified at trial that granules are a typical type of multiparticulate pharmaceutical composition. (5/9/11/ AM tr. at 140). Dr. Williams identified numerous prior art literature references that describe granules as a conventional example of a multiparticulate pharmaceutical formulation. (5/9/11 AM tr. at 146-151). Dr. Williams further testified that he has not seen any scientific literature stating that granules are not multiparticulates or any literature stating that only certain types of granules are multiparticulates. (5/09/11 AM tr. at 153). While these articles are similarly directed to the general definition of a multiparticulate and not the patentee's lexicography, they show that multiparticulates, as the term is normally used, include *some* granules. However, none of them show that all granulations or dry roller compaction are multiparticulates. Thus, while the Court has concluded that the granulation is a multiparticulate, it does not rely substantially on Dr. William's testimony.

Acorda also points to several documents produced by Apotex, where it alleges that Apotex admitted that its product was a multiparticulate.[3] The Court finds that one of these is entitled to some weight.

Acorda points to Apotex's superseded interrogatory response that states, in defense of claims 7-9 and 16-18, that "[e]xpanding the scope of these claims to include *non-bead multiparticulate formulations, such as those contained in Apotex's accused products*, would impermissibly vitiate a clear claim limitation." (PTX 22 at 9). This suggests that Apotex's accused products *are* multiparticulates. However, the Court grants this admission limited weight because, on the previous page, Apotex unequivocally asserts that "Apotex states that it will not infringe any claim of the '557 patent because Apotex's proposed ANDA product is not a 'multiparticulate pharmaceutical composition' as that term is defined in the '557 patent." (*Id.* at 8). Thus, taken as a whole, the interrogatory response (which was subsequently superseded) suggested, possibly unintentionally, that while Apotex's product was a multiparticulate, it did not meet the definition of such in the patent. As seen above, the credible evidence suggests that it was within the patentee's definition of the term "multiparticulate pharmaceutical formulation."

[3] Acorda presented two other pieces of evidence that the Court does not credit. The first is a dissolution study by Apotex, which describes its product as "white granular pellets"; however, experts for Acorda conceded that this likely did not represent Apotex's final product. (PTX12; 5/9/11 AM tr. at 14-16). Second, Acorda points to Apotex's Paragraph IV notice letter because Apotex did not assert noninfringement based on the fact that its product was not a granulation. The Court agrees with Apotex that the volume of authority does not require that Apotex assert every defense in its Paragraph IV statement. *See Takeda Chem. Indus., Ltd. v. Mylan Labs, Inc.*, 549 F.3d 1381, 1390 (Fed. Cir. 2008); *Abbott Laboratories, Inc. v. Apotex Inc.*, 725 F.Supp.2d 724 (N.D.Ill. 2010) (using dicta in *Tekeda* to determine that filers are not limited by assertions in their Paragraph IV statements). As such, Acorda's witnesses ask this Court to make the following inference—if Apotex had thought its non-multiparticulate defense was any good, it would have included it in the letter. This, however, is not a reasonable inference because it asks the Court to speculate about Apotex's litigation strategy. It is just as likely that Apotex did not want to reveal its arguments at that time.

Consequently, the Court finds that this product is a multiparticulate pharmaceutical formulation within the meaning of the patent.

3. Acorda Presented Sufficient Evidence to Show that Apotex's ANDA Product Reduces Cmax and Somnolence at Least in Some Patients, but Insufficient Evidence to Show a Reduction of Cmax and Somnolence in a Statistically Significant Number of Patients

The Court finds that Acorda has put forth enough evidence to demonstrate that in *some patients*, Apotex's product will reduce Cmax and thus somnolence. While it failed to show that Apotex's product will reduce Cmax in a statistically significant subsection of patients, the Court's construction did not require statistical significance. Indeed, the Court rejected Apotex's construction that would have required such a showing and instead adopted Acorda's construction. (*See* Doc. Nos. 85, 72-1 (proposed construction of "reduced")).

The credible evidence of the pharmacokinetics of Apotex's product is scant to say the least. However, the Court infers that in at least *some* instances, patients will experience a lower Cmax and somnolence.

The evidence Acorda has put forth in this litigation as to whether Apotex's product reduces Cmax is the label that Apotex has chosen to adopt. Indeed, its experts admitted that that they relied on no other sources. (*See, e.g.*, 5/9/11 AM tr. at 76-77). However, all of the experts agree that the statements in the label and the label's graph report testing from Acorda's product, not Apotex's product. (5/9/11 AM tr. at 86-89; 5/9/11 PM tr. at 94; 5/10/11 PM tr. at 34; 5/12/11 PM at 93). The experts also agree that the pharmacokinetic data of Apotex's product would not be identical to that of Acorda's. (5/9/11 PM tr. 23-24; 5/12/11 PM tr. at 92-93). Further, the alleged bioequivalence of Apotex's product does not necessitate an infringement finding. Such "equivalence" only requires the pharmacokinetic parameter tested to be between 80% to 125% of the branded testing. (DTX150; 5/12/11 PM tr. at 77, 80-83). On the whole, the

Court finds that this information does not credibly reflect Apotex's product.

Despite having been given samples of Apotex's product, Acorda presented no testing of that product to the Court. Indeed, the only testing that was presented to the Court was from a more limited study from Apotex. (5/12/11 PM tr. at 82-89; DTX151). Both parties agree that using this study to draw conclusions about Apotex's reduction in Cmax between the fed and unfed states is not appropriate because it was not the purpose of the study. Proper crossover studies give the same group of patients different treatments at different times to allow each patient to act as his own control and prevent individual differences from affecting the results. (DTX157). Apotex's study was performed as a crossover between Apotex's and Acorda's products in each state, not between Apotex's product in its fed and fasted state. Different subjects were involved in the studies between the fed and fasted state, and each set of subjects may have had different reactions. Consequently, the differences "could have been due to differences in [the] subjects, and not due to differences in fed versus fasted [states]." (5/12/11 PM tr. at 65-66, 79-80, 87).

While both parties acknowledge that the study is flawed for the purpose of using it to draw comparisons between the fed and fasted state of Apotex's product, amazingly, the parties both rely on the study for their purposes. That study, if relied upon, would show that the subjects who took Apotex's product with solid food (high-fat meal) had a *higher* Cmax than the subjects who took Apotex's product in the fasted state. (5/12/11 PM tr. at 82-89; DTX 151). On the other hand, it would show that the formulation resulted in *lower* somnolence. (DTX 151; 5/12/11 PM tr. at 112-118). Thus, it would suggest that Apotex's product does not meet the Cmax limitations, but does meet the somnolence limitations in the somnolence claims. The Court does not find the study to be convincing on either count because it was not designed for

comparison between these states.

With neither of these sources being convincing, the Court finds itself devoid of any evidence that Apotex's formulation decreases Cmax or somnolence in a statistically significant way. This lack of evidence highlights a lack of testing by Acorda, who despite receiving samples of Apotex's product, did not present such testing to this Court. As such, Acorda has not proven that a statistically significant number of people have reduced Cmax on Apotex's product in the fed state.

However, the question is not whether there is a statistically significant number of patients whose Cmax and somnolence are reduced. The parties discussed this issue during claim construction and the Court accepted Acorda's position and found that no statistically significant "reduction" was required for the claim terms. (*See* Doc. Nos. 85, 72-1 at 4 (proposed construction of "reduced")). Thus, if a single patient attains a reduced Cmax from Apotex's product, the product infringes. Here, the Court infers that some patients will attain a reduced Cmax. Acorda's Cmax testing demonstrates that there is high variability from patient to patient in how that patient absorbs tizanidine; 33 out of 89 patients exhibited increased Cmax despite the fact that the mean plasma concentration was lowered with food. (5/13/11 PM tr. at 45; *see also* 5/13/11 AM tr. at 30). The extremely high standard deviation reported in Apotex's study supports the fact that patients react differently to its product as well. (DTX151). Thus, the Court finds it difficult to believe that no patient anywhere would exhibit a reduced Cmax on Apotex's product in the fed state as compared to the unfed state or to the tablet. As a result, Court infers that Cmax will be reduced in at least some patients.

4. Apotex's Label Does Not Evidence a Specific Intent that Physicians, Pharmacists, or Patients Will Directly Infringe

This is a method patent concerning a method of administering tizanidine multiparticulates to patients with food. As such, Apotex's mere sale of tizanidine multiparticulates does not infringe the patent as Apotex does not administer the capsules at all. Acorda's theory of infringement is based upon inducement under 35 U.S.C. § 271(b). Acorda alleges that statements in Apotex's label encourage others to directly infringe the patent. On the basis of several credibility determinations and for the reasons set forth below, the Court finds that the label does not evidence a specific intent to cause others to infringe the patent.

Section 271(b) provides that "whoever actively induces infringement of a patent shall be liable as an infringer." "Inducement requires a showing that the alleged inducer knew of the patent, knowingly induced the infringing acts, and possessed a *specific intent* to encourage another's infringement of the patent." *Vita-Mix Corp. v. Basic Holding, Inc.*, 581 F.3d 1317, 1328 (Fed. Cir. 2006); *DSU Med. Corp. v. JMS Co.*, 471 F.3d 1293, 1304 (Fed. Cir. 2006) (en banc in relevant part) (emphasis added). "[I]nduced infringement under § 271(b) requires knowledge that the induced acts constitute patent infringement." *Global-Tech Appliances, Inc. v. SEB S.A.*, 131 S.Ct. 2060, 2068 (2011).

Indeed, intent requires more than just knowledge that the induced acts constitute patent infringement; it requires that "the inducer . . . have an *affirmative intent to cause* direct infringement." *DSU*, 471 F.3d at 1306 (citing *MGM v. Grokster, Ltd.*, 545 U.S. 913 (2005)) (emphasis added). While "[i]ntent can be shown by circumstantial evidence, . . . the mere knowledge of possible infringement will not suffice." *Vita-Mix*, 581 F.3d at 1328. Such intent cannot be inferred merely based upon selling a product where that product has substantial non-infringing uses. *See Grokster*, 545 U.S. 913, 932-33 ("Conversely, the doctrine absolves the

equivocal conduct of selling an item with substantial lawful as well as unlawful uses, and limits liability to instances of more acute fault than the mere understanding that some of one's products will be misused. It leaves breathing room for innovation and a vigorous commerce."); *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348 (Fed. Cir. 2003) ("Where there are many uses for a product, as the record reflects to be true of gabapentin, and fewer than 1 in 46 sales of that product are for infringing uses, we are not in a position to infer or not infer intent on the part of Apotex without any direct evidence.").

In this case, the Court finds credible evidence put forth by Apotex that show that there is a substantial non-infringing use for the product, and thus more than the mere sale of the product is required. *See Warner-Lambert Co.*, 316 F.3d 1348. The non-spasticity related, and thus non-infringing, uses of the drug are "approximately 75%." (Librie Tr. at 67). This figure was put forth by Acorda's Vice President of Sales and Marketing, a person who would have no incentive to inflate it. Further, that figure is supported by internal Acorda documents that show the numerous conditions that tizanidine is prescribed for beyond spasticity. (DTX38 at 8-11; DTX 47 at 2-4; DTX 188 at 4-5). Indeed, the infringement is substantially smaller than this number given the pharmacokinetic data before the Court. Both parties testified that even the pharmacokinetic data for Acorda's capsule showed that in the 101 study on the tizanidine-on-beads formulation, there were 33 out of 89 respondents where the Cmax for the capsule in the fed state was *higher* than the Cmax in the fasted state. (5/13/11 PM tr. at 45; *see also* 5/13/11 AM tr. at 30). These patients experience the opposite result to that reported in the patent. Further, such a result would be expected to be observed at an even higher rate in Apotex's product, because, while the values found in Apotex's ANDA study cannot be directly compared because they were performed on different subjects, for tests with the same subjects, Apotex's

product had a higher median Cmax for its fed state, and a lower median Cmax for its fasted state than did Acorda's. (DTX 151). This suggests that even fewer patients would exhibit a lowered Cmax. Thus, the Court concludes that the vast majority of uses of this drug are non-infringing and Acorda must show substantially more than just the sale of the product to evidence inducement.

The question of whether instructions such as those in a generic drug label are convincing evidence of such intent is somewhat unsettled. *Grokster* certainly suggested that some instructions could be when it found that:

> Evidence of "active steps . . . taken to encourage direct infringement" such as advertising an infringing use or *instructing how to engage in an infringing use*, show an affirmative intent that the product be used to infringe, and a showing that infringement was *encouraged* overcomes the law's reluctance to find liability when the defendant merely sells a commercial product suitable for some lawful use.

545 U.S. at 936 (emphasis added). Further, in *Astrazeneca v. Apotex*, 633 F.3d 1042, 1058 (Fed. Cir. 2010), the Federal Circuit affirmed a district court's decision that a drug label that instructed an infringing use was sufficient evidence to infer the generic's intent even though the FDA generally "requires" the generic to copy the label. In that case, the Federal Circuit confronted the issue of whether a label induced infringement of a patent directed to once-daily dosing. The statements in the label directed dosing twice-daily for two of three of the drug's indications at the minimum .25 mg dose. The Federal Circuit also set forth other aspects of the label:

> [I]n its DOSAGE AND ADMINISTRATION section, the label states that "[i]n all patients, it is desirable to downward-titrate to the lowest effective dose once asthma stability is achieved" and "[o]nce the desired clinical effect is achieved, consideration *should be given to tapering to the lowest effective dose*." The PRECAUTIONS section also warns that "suppression of HPA function may be associated ... when the dose is not titrated to the lowest effective dose" and "[t]o minimize the systemic effects of orally inhaled corticosteroids ... each patient *should be titrated* to his/her *lowest effective dose*."

Id. at 1047 (emphasis added). The Federal Circuit determined that it was not clearly erroneous for the district court to find inducement because physicians and patients, faced with a minimum .25 mg dose that was recommended twice-a-day for certain conditions, would titrate down to once daily as the *first step* in downward titration. *Id.* at 1057, 1060. The Federal Circuit approved the district court's inference of intent, not merely based on the presence of the statements in the label, but based on Apotex's[4] decision to go forward with a label that it knew created an infringement issue. *Id.* at 1060. The Federal Circuit so found despite the fact that Apotex had attempted, without success, to carve-out the offending portions of the label. The court determined that because Apotex had still moved forward with the label with knowledge of the issue and without appealing the FDA's decision, filing a Paragraph III certification, or the myriad of other actions available to it. *Id.* Thus, it is clear that labels that give recommendations that would lead inevitably to infringement can give rise to an inference of specific intent.

On the other hand, there is no doubt that, despite the fact that instructions might allow a factfinder to infer intent, such instructions do not in all cases require the inference. Indeed, in *Vita-Mix*, the Federal Circuit determined *as a matter of law* that the defendant's instructions, which when followed could have resulted in infringement, did not evidence inducement. In *Vita-Mix*, the plaintiff alleged that Basic marketed a blender in a way that induced the user to infringe its method patent. 581 F.3d 1317, 1324-25 (Fed. Cir. 2009).

The patent covered a method of using a plunger to prevent an air pocket from forming in a blender, but did not cover the prior art of stirring to destroy already-formed air pockets. *Id.* Basic's blender had a stir stick that was inserted into a hole in the blender lid and allowed the user to stir by swiveling the stick around the edges of the blender.

4 Apotex, the defendant here, was also the defendant in the *Astrazeneca* case.

Vita-Mix argued direct infringement based on a demonstration by Basic's spokesman on a television program where he allowed the blender to run without moving the stir-stick. *Id.* at 1325. Vita-Mix presented an expert, Dr. Swanger, who testified that when the stir stick was not moved, it prevented the formation of air pockets and violated the patent. *Id.* at 1325-26. The district court found, at summary judgment, that Basic's blender did not infringe the patent either directly or by inducement and discounted the testimony of Dr. Swanger. The Federal Circuit reversed because it found that there was a material fact as to whether the blender violated the patent when the stick was left in place.

However, even faced with instructions to turn the blender on and off without suggesting stirring (potentially infringing) and separate instructions to stir with the stir-stick (non-infringing), the Federal Circuit affirmed the no inducement holding as a matter of law. *Id.* at 3335 (Bryson, J., dissenting). The court stated:

> The dissent suggests that Vita-Mix introduced enough evidence to show that following Basic's product instructions *may lead to infringing uses of the device*. The question is not, however, whether a user *following the instructions* may end up using the device in an infringing way. Rather, it is whether Basic's instructions teach an infringing use of the device such that we are willing to infer from those instructions an affirmative intent to infringe the patent. The district court correctly found that Basic's directions do not *even disputably* indicate such intent.

Id. at 1317 n.1 (emphasis added). As a result the Court affirmed the district court's summary judgment against Vita-Mix.

From these cases, the Court determines that instructions can lead to an inference of specific intent, particularly when they specifically direct infringement or lead necessarily to infringement. However, whether the Court makes such an inference depends on how explicitly

the instructions suggest the infringement, any direct evidence, the Court's fact-finding conclusions and the surrounding circumstances.

Acorda has attempted to make this case with Apotex's proposed label. The label contains several statements. These statements do not direct a physician or patient to adminster the capsules with food, but they do give physicians or patients information about issues of switching from the capsule to the tablet. Given the surrounding circumstances, these statements are not sufficiently explicit to evidence induced infringement.

First, the label twice directs the physician to the pharmacokinetics section of the label for information on the *differences* between the fed and fasted states with capsules and tablets. In the initial all-caps warning, the label states:

> PHARMACOKINETIC DIFFERENCES BETWEEN TIZANIDINE HYDROCHLORIDE CAPSULES AND TIZANIDINE HYDROCHLORIDE TABLETS: TIZANIDINE HYDROCHLORIDE CAPSULES ARE NOT BIOEQUIVALENT TO TIZANIDINE HYDROCHLORIDE TABLETS IN THE FED STATE. THE PRESCRIBER SHOULD BE THOROUGHLY FAMILIAR WITH THE COMPLEX EFFECTS OF FOOD ON TIZANIDINE PHARMACOKINETICS.

(PTX9 at 00087). Also, in the DOSAGE AND ADMINISTRATION section, the label states

> Food has complex effects on tizanidine pharmacokinetics, which differ with the different formulations. These pharmacokinetic differences may result in clinically significant *differences* when [1] switching administration of the capsule between the fed or fasted state, [2] switching between the tablet and capsule in the fed state, or [3] switching between the intact capsule and sprinkling the contents of the capsule on applesauce. (see CLINICAL PHARMACOLOGY: Pharmacokinetics).

(PTX9 at 00104). Neither of these statements direct any action on the part of any physician, but merely call attention to the pharmacokinetics section and the differences between tablets and capsules in the fed and fasted states. Further, their context is related to concerns about

switching between the two, not a preference of one over the other or a direction to use the capsule form in the fed state.

There is a statement about decreased Cmax between the fed and fasted states; however, in context, it again contrasts the tablets and the capsules rather than suggesting using the capsules with food. The relevant portions are produced below:

> ***Pharmacokinetic Differences between Tizanidine Hydrochloride Capsules and Tizanidine Hydrochloride Tablets.***
>
> Tizanidine Hydrochloride Capsules and Tizanidine Hydrochloride Tablets are bioequivalent to each other under fasted conditions, but not under fed conditions.
>
> . . . .
>
> Following oral administration of either the tablet or capsule (in the fasted state) tizanidine has peak plasma concentrations occurring 1.0 hours after dosing with a half-life of approximately 2 hours.
>
> When two 4 mg tablets are administered with food the mean maximal plasma concentration is increased by approximately 30%, and the median time to peak plasma concentration is increased by 25 minutes, to 1 hour and 25 minutes.
>
> In contrast, when to 4 mg capsules are administered with food the mean maximal plasma concentration is decreased by 20%, the median time to peak plasma concentration is increased by 2 hours to 3 hours.

(PTX9 at 00089) (emphasis in original). This is accompanied by a graph showing data that appears to support the statement.[5] As can be readily observed, while a decrease in the peak plasma concentration is mentioned, its context in the patent is directed to a comparison with tablets to capsules, and does not suggest that capsules be used in the fed state.

[5] Dr. Myers credibly testified that the graph actually does not show a lower Cmax. Rather, it shows the *average* plasma concentration over time. This does not demonstrate a lower average Cmax because two individuals could reach Cmax at different times. Thus an average of the Cmaxes is not achieved by averaging each individual time point (as the Cmax for the first person did not correspond in time with that of the other) but by determining Cmax and averaging those numbers, regardless of when it was achieved. However, regardless of what the graph actually

Considering all the evidence, the Court finds that Acorda has not shown that this label will induce infringement of either the somnolence claims or the Cmax claims. First, with respect to somnolence, as Acorda's witnesses admitted, the label nowhere says that somnolence is reduced when capsules are given with food or in any situation. (5/9/11 AM tr. at 91-92; 5/9/11 PM tr. at 18-19; 5/10/11 AM tr. at 52, 57, 71). Indeed, Apotex's label only warns patients that they might *experience* somnolence when taking tizanidine capsules (whether with or without food). (PTX4 at 3; PTX9; 5/9/11 AM tr. at 93; 5/9/11 Tr. at 129; 5/10/11 PM tr. at 8-9). Its only statements are that somnolence is a frequent effect and that such side effects appear to be dose related. This is because the FDA does not permit Acorda or Apotex (who was required to copy the label) to sell tizanidine capsules with a label stating that taking the product with food reduces somnolence. (5/10/11 AM tr. at 56-57; Librie Tr. at 161-162). Acorda's internal documents state as much—the capsules have "not demonstrated in a clinical trial" that they reduce somnolence. (DTX 27 at 2-4, ¶¶5, 7, 10, 12). A label devoid of any information directly explaining reduced somnolence of the capsule with food cannot be said to encourage infringement in the surrounding context of this case.

The Court does not find the testimony of Dr. Thrower, Acorda's expert, to be convincing. Dr. Thrower testified that doctors, pharmacists, patients and others would understand from Apotex's package insert that administering Apotex's generic tizanidine capsules with food will reduce Cmax and thereby reduce side effects, including somnolence. (5/9/11 PM tr. at 49; PTX9). Dr. Thrower explained that based on his reading of the label, the optimal way to take Apotex's formulation is to take the capsule with food. (5/9/11 PM tr. at 58). Dr. Thrower further explained that a slower onset of action would reduce somnolence because it allows the

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shows, it certainly appears to show a lower Cmax.

brain and the body to counteract the increase in the drug present in the system. (*Id.* at 64). As such, Dr. Thrower concluded that:

> Apotex is putting out a product with a label that tells the physician to prescribe their capsules with food for the specific purpose of reducing the Cmax, lengthening the Tmax and reducing somnolence. The pharmacist will dispense it with those instructions, will explain it to the patient, and the patient will take the drug under those—we hope under—following those instructions, or as is much more common, the patient will go online and look up the drug and learn about that as well as from direct experience.

(*Id.* at 78). However, the Court does not find this testimony to be credible. Dr. Thrower was entirely conclusory in his analysis and did not explain how a physician or a patient, based on their relative skills, would go forward to infringe the claims. Indeed, rather than engage this analysis, Dr. Thrower substitutes a mischaracterization of the label—as discussed above, the label does not instruct the physician to prescribe in any way. This is because the FDA has expressly prevented Acorda from doing so. (Librie Tr. at 144, 161, 177-78; 5/10/11 AM tr. at 50-51). Rather, the label provides information that a physician can draw upon.

While Dr. Thrower seems to suggest that a physician could "figure it out," there are two problems with that statement. First, Dr. Thrower's analysis was not that of a ordinary doctor, who Acorda alleges will directly infringe the claims.[6] Dr. Thrower is a paid member of the Zanaflex Capsules Speakers' Bureau with knowledge of this drug far beyond the information in the label. (5/9/11 AM tr. at 68-74; *see also* 65-66, 74-75). Acorda paid Dr. Thrower to attend a three-day conference in New Orleans for the sole purpose of learning about Zaneflex Capsules and their benefits, and at that conference the information in the label was "expanded upon." (5/9/11 AM tr. at 68-74). He is also an expert in pharmacokinetics and biostatistics, and so has

[6] The Court notes that prescribing doctors are *not* persons of ordinary skill in the art, but because they will be prescribing the capsules, their view of the contents of the label is the relevant inquiry.

substantially more knowledge of what conclusions to draw from the label. Thus, finding this evidence unconvincing, the Court concludes that Apotex will not induce infringement of the somnolence claims.

The Court finds that the same analysis applies for the Cmax claims. The only difference is that while there is no information on the reduction of somnolence, the Cmax statement says:

> In contrast [to tablets], when two 4 mg capsules are administered with food the mean maximal plasma concentration is decreased by 20%, the median time to peak plasma concentration is increased by 2 hours to 3 hours.

But, as noted above, the context of this statement and all of the other statements are about the dangers of switching from capsules to tablets in the fed state, not the benefits of reduced Cmax when using the capsules. Again, that language is not present because the FDA did not allow the instructions to use the capsule with food to reduce Cmax to be put in the label. While the FDA is not the ultimate arbiter of patent claims, *AstraZeneca*, 633 F.3d at 1061, here it has allowed a label that does not lead inexorably to infringement. Instead, the label alerts the user to switchability issues, not the benefits of reduced Cmax.

While the Court might in some cases find such a label to evidence specific intent, here, the circumstances strongly indicate the opposite conclusion. First, as mentioned, the scope of infringement is minor: 75% of prescriptions are not for spasticity, and likely a large portion of Apotex's capsules that are so prescribed do not infringe the patent. As such, it makes little sense for Apotex's intent to be to infringe the patent rather than to sell a commodity where the vast majority of sales are non-infringing. Second, as mentioned, there is no explicit instruction to use the capsules with food to reduce somnolence and it contains absolutely no information that a physician can even reduce somnolence by using the capsule with food. The Court is unwilling to infer intent based upon information that must be pieced together in a puzzle and where it is

clear that many physicians are unable to put together such information, particularly where the potentially infringing use is such a small subsection of the market. *See Warner-Lambert Co.*, 316 F.3d at 1356. On these facts, the Court simply does not believe that an inference of specific intent is justified.

The label does not direct infringement, and while the information might allow people to infringe, the ultimate question is not whether some physicians may infringe the patent.[7] The question, as stated in *Vita-Mix*, is whether the Court, with its fact-finding capabilities, finds specific intent on the part of Apotex. The Court finds that there is no such intent for either the reduction of somnolence or Cmax. Acorda will of course have the ability to sue for induced infringement if Apotex later puts forth other promotional materials or otherwise promotes its product for reduced Cmax or somnolence.

III. INVALIDITY

Among other theories, Apotex alleges that the patent claims are invalid because they are not enabled to their full scope and that they are obvious. The Court finds that the claims are not enabled to their full scope and, having so found, does not find it necessary to consider obviousness.

A. The Patent Claims Are Not Enabled to Their Full Scope

Apotex alleges that the patent is not enabled for several reasons: (1) because the studies conducted were only on the tizanidine-on-beads formulation, but the purported scope of Acorda's invention extends to all multiparticulates, including conventional granulations; (2) it

[7] The marketing studies suggest that some doctors who were given similar information by phone or who had not been cased by workers got the message, though others clearly did not. (PTX255 at ACO 35288-92; 5/10/11 AM tr. at 104-105; DTX94 at 5, 15-19).

would take undue experimentation to determine what kind of solid foods a multiparticulate would actually cause a decrease in Cmax and somnolence; (3) there are a substantial number of inoperative embodiments of the claims because the timing of the meal and taking the drug would have to be well-coordinated, but the claims reach a scope of administration where no reduction in Cmax or somnolence would occur.

The Court agrees and finds that the limited scope of the study supporting this invention, particularly in that it was only ever conducted with the tizanidine-on-beads formulation, and the extremely wide breadth of the claims with respect to multiparticulates demonstrate that the invention was not enabled to its full scope.

1. Law Applicable to Enablement

The enablement requirement is codified in 35 U.S.C. § 112, ¶ 1, which states:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, *to make and use the same*, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(Emphasis added). The purpose of the enablement requirement is to ensure that the inventor has fulfilled his side of the bargain in order to obtain the patent monopoly. *Invitrogen Corp. v. Clontech Labs.*, 429 F.3d 1052, 1063 (Fed. Cir. 2005); *Lizardtech*, 424 F.3d at 1344 (this element is the "quid pro quo" of the patent bargain). The inventor has done so only if he has described the invention in a way that a person can make and *use* that invention. *Id.*; *see also In re Wands*, 858 F.2d 731 (Fed. Cir. 2008); *Ariad Pharm.*, 598 F.3d 1346 (the purpose of the enablement requirement is to "require the patentee to describe his invention so that others may construct and use it after the expiration of the patent"). To satisfy the enablement requirement, a specification must teach those skilled in the art how to make and to use the full scope of the

claimed invention without undue experimentation. *Genentech*, 108 F.3d at 1365. "While every aspect of a generic claim certainly need not have been carried out by the inventor, [8] or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." *Id*. at 1366.

A claim is not invalid merely because some experimentation is necessary to practice it; however, such experimentation "must not be unduly extensive." *Atlas Powder Co. v. E.I. Du Pont de Nemours & Co.*, 750 F.2d 1569, 1576 (Fed. Cir. 1984). A court may consider several factors in determining whether undue experimentation is required to practice a claimed invention, including: (1) the quantity of experimentation necessary; (2) the amount of direction or guidance disclosed in the patent; (3) the presence or absence of working examples in the patent; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (6) the predictability of the art; and (7) the breadth of the claims. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). These factors are sometimes referred to as the "Wands factors." The application of these factors is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed. *PPG Indus., Inc. v. Guardian Indus., Corp*., 75 F.3d 1558, 1564 (Fed. Cir. 1996).

A related inquiry examines the presence of inoperative embodiments and informs the enablement inquiry. *National Recovery Techs. Inc. v. Magnetic Separation Sys., Inc.*, 166 F.3d 1190, 1196 (Fed. Cir.1999). While a claim is invalid for lack of enablement "if it reads on a

[8] Indeed, the specification need not teach what is well known in the art. *Hybritech v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir.1986).

significant number of inoperative embodiments," the fact that there are many inoperative embodiments does not make the claim fail enablement "if the necessary information to limit the claims to operative embodiments is known to a person of ordinary skill in the art," *Crown Operations Int'l, Ltd. v. Solutia Inc.*, 289 F.3d 1367, 1381 (Fed. Cir. 2002) (internal citations omitted).

Because patents are presumed valid, lack of enablement must be proven by clear and convincing evidence. *See Auto. Tech. Int'l, Inc. v. BMW of N. Am., Inc.*, 501 F.3d 1274, 1281 (Fed. Cir.2007); *AK Steel Corp. v. Sollac & Ugine*, 344 F.3d 1234, 1238-39 (Fed. Cir.2003).

Here, the Court finds, by clear and convincing evidence, that the undue experimentation would be necessary to practice the claimed invention to its full scope because it is impossible to determine what "multiparticulate" formulations would produce the claimed effect. Further, the Court finds that additional experimentation would be necessary to determine what kind of food was sufficient to gain the effect.

A claim must be enabled to its full scope. This means that it needs to be enabled to the same extent that it is extended during the infringement analysis. In this case, Acorda requested the broad constructions at issue. The Court adopted Acorda's construction that statistical significance was not required to show infringement of the patent based on the instrinsic evidence. (*See* Doc. No. 72-1 at 4). The Court further adopted Acorda's construction of granulation. (*See* Doc. No. 72-1 at 15). As a result, Apotex may show invalidity by demonstrating by clear and convincing evidence that a person of ordinary skill would not be able to determine with any certainty whether such method would succeed in a given person. Further,

Apotex may show that a person of ordinary skill would not be enabled from the patent's disclosure to practice the patented method with a dry granulation.

2. Wand Factors

The *Wands* factual factors support the conclusion that the claims are not enabled to their full scope. The Court finds that it would require undue experimentation to formulate a roller-compacted formulation or other similar dry granulation to practice the claimed invention.[9] Further, the Court determines that the timing of the food and amount and quality of food given contribute somewhat to the experimentation required.

a. The Breadth of the Claims

The claims at issue are very broad. As set forth above, they apply even to a dry roller-compacted granulation, which includes substantial powder. Whether or not it is also a "multiparticulate" within the meaning of the patent, there is no question that there are substantial—pharmaceutically relevant—differences between sprayed beads (*see* '557 patent 9:45-62), and a roller compacted granulation. The presence of substantial fine powders certainly

[9] The Court does not rely on Dr. William's assessment of applesauce as an inoperative embodiment because it finds that applesauce is not a "solid food" within the meaning of that term. (*See* 5/13/11 PM tr. at 34). Nor does the Court rely on the argument that the cognitive assessment tests did not measure somnolence because it finds credible Dr. Zammit's testimony that the tests were often used for such determinations and that the factors Dr. Fink used to undermine their reliability were not present in this experiment. (5/20/11 AM tr. at 109). Dr. Zammit was the only expert qualified at trial to assess the somnolence studies, and the Court finds his testimony on the matter to be credible. (5/20/11 tr. at 91-92; '557 patent, 7:19-40; 5/09/11 PM tr. at 61-62; PTX1 at col. 6:46-61). The patent and the studies disclose a reduction in somnolence at 0.75 hours for the fed-capsule, and, while the other data do not evidence a reduction, a reduction that this time point is sufficient.

would suggest that the drug product would dissolve and disperse quite differently in the stomach and intestinal tract.

The claims also apply broadly to virtually any type of food that the patient could eat with the dosing. They apply to any "solid food," a construction proposed by Apotex, not just the type of food tested. (Doc. No. 72-1 at 17). Finally, some of the claims are broad with respect to the timing of taking that food, allowing a patient to take the tizanidine up to 1 hour before, to two hours after the food. (Doc. No. 85). Finally, the claims are broad in that they may be infringed even if a single person exhibits a lower Cmax. Thus, there must be disclosure to determine whether such a person would in fact exhibit those characteristics.

b. The Relative Skill of Those in the Art

The level of skill in the art for this patent is substantial. At trial, the parties agreed that the relevant art was that of pharmaceutical formulation in November of 2001 (the filing date of the '557 patent). The parties further agreed that the person of ordinary skill in the at art would have a Ph.D. in pharmaceutical sciences, or a related field, with three to five years of experience in the pharmaceutical industry, or an appropriate bachelor's or master's degree and about seven years of experience formulating drugs. (5/11/11 PM tr. at 51-52; 5/23/11 AM tr. at 23-24). Thus, a person of ordinary skill had substantial skill.

c. Predictability of the Art

The Court finds that pharmaceutical formulation is generally an unpredictable art. Changes in excipients, formulation method, and other details of formulation, including the preparation of the capsule by one method and not another, result in substantial changes in the

pharmacokinetic profile. (*See* 5/23/11 AM tr. at 42-44; 5/13/11 AM tr. at 19-21; 5/12/11 AM tr. at 12-15).

d. Amount of Direction or Guidance Disclosed in the Patent and Working Examples and the Amount of Testing Necessary

The Court finds that, even when viewed from the perspective of a person of ordinary skill in the art, the patent provides very little guidance. The test disclosed merely shows the results for one type multiparticulate—tizanidine on beads. (*See* 5/12/11 AM tr. at 69-70). Thus, it is difficult even to project out to other multiparticulates. The patent discloses no information about what it is about multiparticulates that would result in the reduction of Cmax. In this regard, the Court finds Dr. Jarosz's testimony that moving from a bead to a roller compaction granulation would be unpredictable.

With respect to working examples, the patent does provide substantial evidence of five different examples of the tizanidine-on-beads formulation. The examples disclose five different ways of making tizanidine on beads, using different excipients and amounts by weight. ('557 patent at 9:25-13:42). All of those examples, however, are in the form of tizanidine-on-beads formulations and do not extend to the other possible covered multiparticulates.[10] (*See* '557 patent at 9:25-13:42).

With respect to the timing of food and type of food, the conditions in the 101 study, disclosed in the patent, the patients took the preferred tizanidine-on-beads composition at the same time they ate a high-fat meal—two fried eggs, two strips of bacon, two slices of toast with butter, a hundred grams of hash browns and one glass of whole milk. (DTX 25 at 22-23; 5/13/11

AM tr. at 12-14). Whether these could be expanded to the scope of any solid food, as the Court's construction requires, or could be generalized to taking the dose an hour before the food, also required by the construction, is unclear.

Further, the testimony of Acorda's own experts suggest that a party could not expect to practice the claimed invention with another formulation and that substantial testing was necessary. Acorda's expert, Dr. Williams, testified that he has no idea how any multiparticulate composition, even the preferred tizanidine-on-beads composition, works in reducing Cmax or somnolence. (5/23/11 AM tr. at 73-74, 81-82). How then, could a person of ordinary skill determine what it was about a multiparticulate in order to apply that to another formulation? Indeed, Acorda's expert Dr. Slotkin was unable to point to any portion of the patent that explained to one of skill in the art what aspect of multiparticulates caused the lower Cmax. (5/23/11 AM tr. at 82-85). Further, Dr. Slotkin testified that the results of the tizanidine-on-beads formulation could not have been predicted beforehand. (5/9/11 AM tr. at 52-53). This strongly suggests that the data for another formulation—a granulation multiparticulate—would be equally difficult to predict. Further, given the substantial powder and apparent dissolvability of much of Apotex's roller-compaction granulation, there is little reason to believe that it would act in a similar way to beads prepared on non-pareil seeds.

Dr. Williams' testimony to the contrary is not persuasive. Dr. Williams testified only that "one of skill in the art would be very versed in how to make a granulation, how to make granules by a variety of different means, it's a conventional process. There's ample guidance given in the '557 patent, as I've testified to, so I don't agree with [Dr. Jarosz's] opinion." (5/23/11 AM tr. at

[10] The Court again notes that only one of these formulations was the subject of the 101 study.

59). This answer evaded a question asked by Acorda's own attorney on the more substantive issue of whether there would be difficulty in formulating a granulation with the particular pharmacokinetics claimed in the patent. (*Id*.) Further, Dr. Williams' testimony was inconsistent with the testimony of Acorda's other experts above.

Further, the results of the 101 study are not so convincing that a person of skill in the art could have concluded that, for a given patient, the claims would result in a reduced Cmax, particularly with a formulation that includes substantial powder. Dr. Slotkin testified that even in the 101 study on the tizanidine-on-beads formulation, there were 33 out of 89 respondents where the Cmax for the capsule in the fed state was *higher* than the Cmax in the fasted state. (5/13/11 PM tr. at 45; *see also* 5/13/11 AM tr. at 30). Dr. Myers testified that this would result in difficulty making a prediction on whether an individual patient would have the same reaction as the majority of patients in the study. (5/12/11 PM tr. at 71). Dr. Thrower's testimony to the contrary—that he has successfully practiced the '557 patent claims under more general conditions in his practice—is not convincing, as it contradicts this testing, which suggests that for many patients he would observe the opposite effect. Dr. Slotkin's similar argument (5/13/11 PM tr. at 93-96), is also not persuasive because with the large number of people who reported increased Cmax, it makes little sense to expect changes to report *only* a reduced effect for these people—some people on the border will undoubtedly cross the line. Indeed, Dr. Slotkin partially conceded this point at deposition. (5/13/11 AM tr. at 96).

Thus, the Court concludes that the amount of testing necessary to practice the invention would have been substantial. Dr. Meyer testified that one would need a statistical analysis of clinical data from studies varying the type and timing of food to understand whether Cmax

would be reduced in different conditions. (*See* 5/13/11/ AM tr. at 32-35; *see also* 5/13/11 PM tr. at 96). If this was required for changing the eating conditions, it certainly would be required to determine whether a particular granulation, which has substantial differences from the beads formulation, would result in a decreased Cmax and the resultant reduction in side-effects.[11] This was supported by the fact that the FDA recommends food effect testing be repeated any time a change is made to a formulation. (PTX230 at 3). This would have to be repeated for each roller compacted granulation that was painstakingly formulated in an attempt to reproduce these effects.

Finally, the timing of the food and the amount of food required would result in additional required testing—the 101 study involved a high-fat meal and immediate dosing after it. While the testing on this front might be more predictable, it adds to the amount of testing required.

e. The State of the Prior Art

The state of the prior art does give substantial guidance to a person of ordinary skill in the art. First, the Digenis Article provides substantial guidance to one of ordinary skill in the art of multiparticulates as far as reducing the Cmax values of pharmaceutical formulations. The article teaches substantial information about the effects of using an erythromycin multiparticulate formulation. (DTX9 at 14-15, 17; 5/12/11 AM tr. at 26, 31-32). The Digenis article maps an experiment where blood plasma levels of the drug and its location in several patients' GI tracts are observed using irradiated beads. The article observes that lower

[11] Certainly Bernard Sher's deposition suggests considerations that would guide people of exceptional skill in the art who might try to increase the likelihood of making a *bioequivalent* drug. However, the task of making bioequivalent drug is different than making one that infringes.

bioavailability and lower Cmax are observed in patients who take the beaded multiparticulate with food. (DTX9 at 17). The article also cites another study where the capsule multiparticulate erythromycin had its blood plasma levels reduce substantially under fed conditions. (*Id.* at 22).

Further, the '745 patent discloses that when morphine sulfate layered on beads was ingested with food, the peak plasma concentration decreased compared to morphine in a tablet form taken without food. (DTX16 10:12, Table 2; 5/1211 AM tr. at 36). However, both of these references deal only with beaded multiparticulates and not with the dry granulation that must be formulated.

f. Conclusion

Based on the foregoing analysis, the Court finds that, particularly with respect to a non-beaded dry granulation (including powders), the scope of the claims is not fully enabled. The testing would be substantial, iterative testing involving experiments such as those prepared for the NDA or the ANDA, with large enough sample sizes to be considered legitimate by the experts before the Court. (PTX230 at 3; *see* 5/13/11/ AM tr. at 32-35; see also 5/13/11 PM tr. at 96). Indeed, even the bioequivalence testing in the ANDA was criticized by Acorda as inadequate to base conclusions on. Additional testing would be required to determine the scope of type of food that could be taken to achieve the effect of the invention in a given person. Thus, by clear and convincing evidence, the Court finds that the claims are invalid because they require undue experimentation to practice to their full scope.

B. Obviousness

Having found the patent not enabled, the Court sees no reason to address obviousness, an alternative ground for invalidity.

C. Written Description

The Court, having heard the evidence of the parties, finds that Apotex has failed to carry its burden of proving lack of written description by clear and convincing evidence. Essentially the question is whether "multiparticulate" encompassed a granulation within the original meaning of the patent. The Court finds that such a description was supported for the same reasons as the granulation is considered to be within the scope of the claim. There is no lack of description in the specification for the claim scope—indeed, the claim term's inclusion of a granulation came directly from its express definition in the specification. As such, the Court concludes that it is unable to find, by clear and convincing evidence, that the claim term was not present in the specification.

V. ADDITIONAL CONTENTIONS OF THE PARTIES

Apotex argues both that the claims are not directed to patentable subject matter under 35 U.S.C. § 101 and that the claims here require a multiple actor theory, which they allege has not been proven. These allegations are related. Apotex argues that the claims require multiple actors because no one actor can carry out the claims because a physician can only prescribe, he cannot force the patient to take the medication with food. On the flip side of the coin, Apotex argues that this construction leads to unpatentable subject matter because if the patient does not ultimately take the capsule with food, the claim is to a mental process. The Court disagrees on both counts.

A. The Court Finds that the Patent Claims Involve Patentable Subject Matter

The Patent Act provides "[w]hoever invents or discovers any new and useful process,

machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor . . . ." 35 U.S.C. § 101 (2006). This case involves a process, which § 100(b) defines as a "process, art or method, and includes a new use of a known process, machine, manufacture, composition of matter, or material." *Id.* § 100(b). To be a patent eligible process, the predominant test, termed the "machine or transformation" test, provides that a process is patentable upon a showing that the claim is tied to a particular machine or transforms an article. *Gottschalk v. Benson*, 409 U.S. 63, 70 (1972).

But in *Bilski v. Kappos*, the Supreme Court, in interpreting §§ 101 and 100(b), reversed the Federal Circuit's holding that the "machine or transformation" test is the exclusive test for determining whether a process is patentable. *See* 130 S.Ct. 3218, 3227 (2010). While that test is a helpful tool in the § 101 analysis, the Supreme Court found that the test reads language into the statute and limits the ordinary, contemporary, and common meaning of "process." *Id.* at 3225-26. Ultimately, *Bilski* applied, not the machine or transformation test, but the Court's precedent on the exclusion of abstract ideas from § 101 patentable subject matter. *Id*. at 3229-31. "A principle, in the abstract, is a fundamental truth; an original cause; a motive; these cannot be patented, as no one can claim in either of them an exclusive right." *Benson*, 409 U.S. at 67. That analysis is based on the claims viewed as a whole; it is irrelevant that claim limitations viewed individually are patent-ineligible. *See Parker v. Flook*, 437 U.S. 584, 594 (1978).

In this case, the parties disagree over whether the '557 patent claims patentable subject matter. Apotex proceeds on the premise that the patented methods are fully performed by the mere prescribing or dispensing of the drug. (Def.'s Br. at 38; Doc. No. 275). As such, it contends that the '557 patent covers no more than a non-transformative mental process, which is

non-patentable subject matter. (*Id.*).

The Court disagrees. The '557 patent claims more than Apotex suggests. Specifically, in addition to administering the drug, the claim limitations further require the giving, dosing, self-dosing or taking of the composition resulting in "a peak plasma tizanidine concentration earlier than about 4 hours from administration" or similar limitation. Apotex is wrong to proceed on the premise that the'557 patent is limited to a one-step mental thought process. Rather, the '557 patent expressly requires a physiological effect on the human body in the form of reduced peak plasma or somnolence; in other words, the claims require a transformation. To analyze the claims without this limitation would result in the Court impermissibly determining eligibility on only one of several claim limitations embodied in the '557 patent, which is improper. *See Parker*, 437 U.S. at 594. If the patient does not ultimately take the drug, then the tizanidine therapy will not result in reduced Cmax or somnolence as required by the claims and will not be a practice of the claimed invention. Thus, read with all of its required limitations, the '577 claims encompass more than the mental process of prescribing or self-dosing; the claims describe a method for the treatment of patients resulting in a physiological change. As such, the '557 claims are not a patent-ineligible mental process. Furthermore, the claims satisfy the machine or transformation test because the step of "administering" the drug with food results in the transformative step of producing a peak plasma tizanidine concentration or a somnolence effect. Therefore, the '557 patent claims disclose patentable subject matter.

B. Multiple-Party Infringement Theory

In order to present a successful claim for inducement to infringe under § 271(b), there first must be direct infringement of the patent. *See Dynacore Holdings Corp. v. U.S. Philips*

Corp., 363 F.3d 1263, 1272 (Fed. Cir. 2004). Direct infringement requires a single party to perform every step of a claimed method. *See BMC Res., Inc. v. Paymentech, L.P.*, 498 F.3d 1373, 1380 (Fed. Cir. 2007). However, it would be unfair to allow a party to avoid liability by having someone else perform a patented step. *Id.* at 1379. Accordingly, in a case in which more than one party is performing the claimed method, a court may find liability if the defendant exercises "control or direction" over the entire process such that every step is attributable to him. *Id.* at 381.

The parameters of the "multiple party infringement theory" have not been developed extensively. In *Muniacution Inc. v. Thomson Corp.* and *BMC Resources v. Paymentech*, the Federal Circuit reasoned that sufficient "control or direction" exists where the defendant contracts out steps of the process or is otherwise vicariously liable for the actions of the other party. *See* 532 F.3d 1318, 1330 (2008); 498 F.3d at 1381. Most recently, in *McKesson Technologies* and *Akamai Technologies*,[12] the Federal Circuit held that there can be liability for indirect infringement where an agency relationship exists between the parties performing the claimed method. *See McKesson Techs. Inc. v. Epic Sys. Corp.*, 2011 U.S. App. LEXIS 7531 at *9 (April 12, 2011), *vacated*; *Akamai Techs., Inc. v. Limelight Networks, Inc.*, 629 F.3d 1311, 1320 (2010), *vacated*.

The Court need not reach the question of whether Apotex is liable for inducement to infringe under the multiple party infringement theory. A single actor could perform all of the elements of the '557 claims. In light of and consistent with the Court's claim construction of

[12] Both *McKesson* and *Akamai* were vacated and are being considered *en banc*. The issues include the circumstances under which a defendant could be liable for inducing infringement where more than one party performs the claimed method and whether a doctor-patient relationship might affect liability. 2011 U.S. App. LEXIS 10674 (May 26, 2011); 2011 U.S. App. LEXIS 8167 (April 20, 2011).

"administering" and "administration of the composition," a physician, pharmacist, or patient could alone infringe the patent. For example, a doctor could perform the administering of a therapeutically effective amount of tizanidine with food as well as administration of the composition, thereby reducing somnolence in a patient. The patient could read the label, request the capsules from his doctor, and subsequently practice the claimed method. Therefore, because it is possible for one party to directly infringe the claims, and such a situation will likely occur, the Court need not consider multiple-actor theory.

C. Permanent Injunction and Other Issues

Having decided the issues above, the Court finds that these issues are unnecessary to the disposition of this case.

VI. CONCLUSION

For the foregoing reasons, Apotex does not infringe the patent by inducement and the patent is invalid.

Dated: September 6, 2011

/s/ Garrett E. Brown
GARRETT E. BROWN, JR., U.S.D.J.